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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,703	06/27/2000	IAN ROSS DOYLE	017227/0157	9876

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EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/01/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/486,703	Doyle et al
Examiner	**Art Unit**
Patricia A. Duffy	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 29, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3, 4, 6-9, and 11-40* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3, 4, 6-9, 11, 12, and 37-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1, 3, 4, 6-9, and 11-40* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The amendment filed 5-29-03 has been entered into the record. Claims 1, 3, 4, 6, 7, 8, 9, 11, 12 and 37-40 are under examination. Claims 13-36 have been withdrawn as non-elected.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. This application contains claims 13-36 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections Withdrawn

4. The rejection of claims 1-12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons made of record.

Rejections Maintained

5. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of diagnosing lung damage by measuring an increase in pulmonary surfactant A (SP-A) and /or pulmonary surfactant B (SP-B), does not reasonably provide enablement for diagnosing lung damage by measuring decreases in SP=A or SP-B or measuring levels of pulmonary surfactant C (SP-C) or pulmonary surfactant D (SP-D) or decreases in any of SP-A or B. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is maintained for reasons made of record in Paper No. 12, mailed 11-29-02.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that the rationale of the examiner is incorrect and that applicants have discovered that changes in the alveolar capillary membrane permeability lead to leakage of surfactant molecules. This is not persuasive, it is not commensurate in scope with the claims. Applicants have shown that SP-A and/or SP-B can be found in the blood but is devoid of any data relating to SP-C and SP-D. There are no normal or disease levels taught for these other claimed polypeptides. As previously, explained the correlation is a critical feature of the invention and this correlation with an increase is not taught by this specification and Applicants have provided no evidence to indicate that the same correlation holds for SP-C and SP-D. The rejection is maintained.

6. Claims 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of monitoring the changes in the extent of lung damages by measuring changes in SP-A and or SP-B , does not reasonably provide enablement for measuring changes in SP-C and/or SP-D. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims is maintained for reasons made of record in Paper No. 12, mailed 11-29-02.

Applicants have not traversed this rejection. Even if Applicants would have traversed this rejection on the same basis as for the enablement rejection as applied to claims 1-7 above, the arguments were not persuasive for reasons set forth in Paragraph 5 of this office action.

Claim Rejections - 35 U.S.C. § 102

7. Claims 1, 3, 4, 7, 8, 9, 38, 39, and 40 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Honda (Japanese Journal of Thoracic Diseases, 34 Suppl. Abstract only, December 1996; reference A11 on PTOL-1449 of 6-6-00) is maintained for reasons made of record for claims 1-5, 7-10 and 12 in Paper No. 12, mailed 11-29-02.

Applicants argue that the methods are drawn to methods of detection of lung damage and not lung disease. This is not persuasive, Honda et al specifically suggest that SP-D and Sp-A, which are primarily secreted from alveolar type II cells into the lumen, can enter the blood stream easily do to injury at the alveolar-capillary membrane (i.e the instant lung damage). Further, the serum SP-D and SP-A concentrations appeared to reflect disease activity of IIP (see abstract). Lung damage is a necessarily a component of idiopathic interstitial pneumonia, a debilitating lung disease and would necessarily be recognized by one skilled in the art. As such, the methods of Honda et al inherently detect lung damage (injury to the alveolar-capillary membrane). As such, there is Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001). Applicants argue that disease and damage are not equivalent. This is not persuasive, for idiopathic interstitial pneumonia lung damage is a necessarily a component of idiopathic interstitial pneumonia. Applicants argues that all lung damage is not due to disease and that these forms of damage may not necessarily form the basis of a screening protocol for disease. This is not persuasive, the claims do not distinguish lung damage generated from disease as opposed to lung damage do to the argued insults (i.e. damaged ligaments or muscles). The fact that some diseases may not be associated with lung

damage does not abrogate the fact that lung damage is necessarily and inherently associated with idiopathic interstitial pneumonia. The claims do not distinguish between lung damage necessarily present in disease and lung damage due to other insults that would not necessarily be "disease". In contrast to Applicants' assertion "Disease" is not necessarily correlated with overt clinical manifestations especially in those individuals with relapsing and remitting disorders such as idiopathic interstitial pneumonia. Applicants argue that the invention provides for a means of monitoring. This is not persuasive, so does the art. Applicants argue that the present invention provides a degree of sensitivity that was not available in the field previously and is not contemplated in the prior art. This again is not persuasive; the claimed invention provides no distinguishing features between the art assay and the claimed assays. The claims are merely drawn to screening for an increase. The art meets this limitation and there is no claimed characteristic of the "screening" to distinguish between the art method and the claimed method. Applicants argue that the art does not teach "early stage lung damage", this is not persuasive, early stage is defined in the specification to include mild but chronic lung damage as such the art of IIP appears to meet this aspect of the definition since it is a chronic disease that has lung damage present and Honda conclude that injury of the alveolar-capillary membrane provides for leakage of SP-D and SP-A into the blood stream. As such, if alveolar-capillary membrane damage is present then, by Applicants own definition this is early stage lung damage as it relates to "mild chronic disease" as set forth on page 9, lines 16-17. As such, the limitation of the claimed invention is met.

8. Claims 1, 3, 4, 7, 8, 9, 38, 39, and 40 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Abe et al (Japanese Journal of Thoracic Diseases, 33(11):1219,

Abstract Only, November 1995; reference A10 on PTOL-1449 of 6-6-00) is maintained for reasons made of record for claims 1-5, 7-10 and 12 in Paper No. 12, mailed 11-29-02.

Applicants arguments have been carefully considered but are not persuasive. Applicants again argue that the methods are drawn to methods of detection of lung damage and not lung disease. This is not persuasive for reasons set forth for Honda et al supra. Applicants assert that the present invention claims the detection of very early stage lung damage or lung damage in asymptomatic patient and facilitates the prediction to developing severe lung damage. This is not persuasive. Abe et al teach that the serum levels of SP-A in patients with IIP and that the SPA-levels correlated closely with the clinical course and rose significantly during exacerbations of IIP (see abstract) and lung damage is a necessarily a component of idiopathic interstitial pneumonia, a debilitating lung disease and would necessarily be recognized by one skilled in the art. Further, the applicants specifically contemplate early stage lung damage as alveolar-capillary damage or "mild" damage in chronic diseases. IIP is a chronic disease. As such, the methods inherently detect early lung damage in IIP exacerbations and further patients with IIP are in fact inherently predisposed to developing lung damage. Applicants argue that the art does not teach "early stage lung damage", this is not persuasive, early stage is defined in the specification to include mild but chronic lung damage as such the art of IIP appears to meet this aspect of the definition since it is a chronic disease that has lung damage present. Applicants argue that it is not possible to draw any correlation with any specific marker with lung damage as opposed to any other manifestation of disease. This is not persuasive, the markers used in the claims are the same as the art and the disease of the art inherently has lung damage and therefore the methods inherently performs the function of screening for lung damage. Lung damage is a necessarily a component of

idiopathic interstitial pneumonia. Applicants argue that not all patients of the prior art had increases in SP-A and therefore all did not have lung damage and therefore no correlation between lung damage and SP-A levels can be made. This is not persuasive, the claims do not require a 100% specificity and sensitivity of the method. This is also not persuasive the methods of the art is performed on a population of individuals with a disease known to cause lung damage. Applicants argue that no such association can be made because 100% of the patients should have exhibited increased levels and is pure speculation on the part of Applicants. This is not persuasive, it is well established in the art that all methods have a false negative and false positive rates, a negative finding is not a determination that disease or damage is not present, it merely reflects the limitation of the assay and does not establish that patients with IIP do not have lung damage. Applicants argue that the art does not recognize or teach that SP-A is correlated with lung damage. This is not persuasive, the art meets the limitation of the claims and further it is well established in the art that IIP has lung damage and the issue is inherency not obviousness (i.e. the instant argued suggestion). There is clear overlap in the claims and the art. Therefore, the detection of SP-A and modulations thereof associated with exacerbations of IIP, necessarily and inherently detects lung damage as claimed. The levels were increased in a body fluid of a mammal in a patient population known to have a disease associated with lung damage and that it could be used to monitor exacerbations. Therefore the art meets the limitations of a mammal predisposed to developing lung disease measures SP-A at a point where clinical symptoms are not apparent (before exacerbation of disease). The rejection is maintained.

9. Claims 1, 6, 7, 8, 9, 11, 12, 37, 38, 39, and 40 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ian R. Doyle (Advances in Critical Care Testing, Eds. List,

Muller and McQueen, Springer-Verlag Telos, January 1997; reference A17 on PTOL-1449 10-18-00) is maintained for reasons made of record for claims 1-12 in Paper No. 12, mailed 11-29-02.

Applicants arguments have been carefully considered but are not persuasive. Applicant again argue that the examiner did not appreciate that the claims are drawn to lung damage and not lung disease. This is not persuasive, the patient population tested by Doyle (i.e. acute respiratory distress syndrome (ARDS) is the same that is specifically identified in the specification at page 2, that is co-incident with lung damage. The art assays the same population of individuals that the specification specifically identifies as having lung damage and uses the same chemical markers. The art teaches that an increase in the marker is observed. Further, Doyle et al specifically appreciated the association of the markers with severity of lung injury. "We concluded that SP-B enters the circulation more readily than SP-A in a manner reflecting the severity of lung injury..." (page 152, see first line of paragraph entitled Conclusions). As such, the art specifically teaches that the levels of surfactant proteins (i.e. the claimed and assayed markers) specifically correlate with the degree of lung injury (i.e. the instant lung damage). Applicants argue that the art does not teach "early stage lung damage", this is not persuasive, early stage is defined in the specification to include chronic lung damage and therefore the art appears to meet this limitation. Applicants argue that the teachings of Doyle et al need to be taken in context of the art of 1994 and that at that time many indicators were being investigated to track the onset of lung damages but these mediators could also have been indicative of other unrelated conditions and does not have the function as an exclusive marker. The fact that multiple markers are found to multiple conditions does not obviate the observation by Doyle that the claimed SP-A and SP-B are markers for lung injury in ARDS

patients. The cited art clearly and unambiguously teaches the association with lung damage of the claimed marker with lung injury in a condition specifically identified in the specification. Specificity and sensitivity of the assay are not probative issues when the claimed invention is clearly anticipated and the claims do not distinguish the assay parameters of the art from the claimed assay parameters. Secondary considerations argued by Applicants are not relevant to an anticipation rejection under 35 U.S.C. 102(b). There is nothing in the claims to distinguish the claimed method from the method of the prior art and as such issues of sensitivity and specificity are moot. Doyle et al specifically teaches the association of the levels of SP-A and SP-B with lung damage in ARDS patients. ARDS patients are clearly contemplated by the specification as filed. It is further noted that Appendix B is not present nor attached to the response. With respect to new claim 39, it is noted that any patient on a ventilator or any patient is "predisposed to developing lung damage". With respect to claim 40, the art meets this limitation because the patients were not reported to exhibit clinical symptoms of any viral infection such as HIV, influenza or smallpox. Because the claim does not specify the clinical symptoms, it encompasses any clinical symptom.

New Rejections Based on Amendment

Claim Rejections - 35 U.S.C. § 112

10. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 40, the recitation of ".. wherein said mammal is not yet exhibiting clinical symptoms." is indefinite because neither the specification nor the claims indicate

what the clinical symptoms are directed to. Is this any clinical symptoms for any disease or clinical symptoms of lung damage. Clarification is requested.

Status of Claims

11. All claims stand rejected.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.

June 27, 2003

Patricia A. Duffy

Patricia A. Duffy, Ph.D.

Primary Examiner

Group 1600